FUNCTIONAL NERVOUS DISEASES AND THEIR RELATIONS TO GASTRO INTESTINAL DERANGEMENTS.[1]

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AS a teacher of the materia medica it has long been my practice to divide all medicines proper into two great classes, namely, the organic and the functional. The organic medicines are those whose special remedial action can never be secured by one dose, but only by the slowly cumulative effects of many repeated doses. The functional medicines, on the other hand, are those whose whole specific action is obtained by one dose, and no repeated doses of them ever effect more than did the first dose. Iron given for anæmia or mercury for syphilis are examples of the organic medicines: opium and belladonna are examples of the functional medicines. The organic medicines are given for the diseases or morbid conditions themselves and not for their symptoms. The functional medicines are given for the symptoms and for nothing else. If, therefore, potassium iodide relieves the pain of a syphilitic node, it is because it removes the node itself. If opium, on the other hand, relieves the same pain, the node still remains to renew the pain so soon as the effect of the dose has worn off. The organic medicines should not produce any symptoms of their own. If they do, they are not producing their remedial effects. The patient should not know that he is taking anything, except by signs of returning health. The functional medicines, on the contrary, do nothing but produce symptoms. Organic medicines show no effects, that is, not the effects for which they are given as remedies, except in states of disease. Iron does not increase the strength of a healthy man, and no healthy man will show any beneficial effects from mercury such as a syphilitic person does. But functional medicines show the same symptoms in health as in disease. Strychnia does not need an invalid to illustrate its properties, and an emetic will act in its proper dose on the most normal stomach.

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Time will not allow still other contrast, to be presented between these two classes of medicines, but what has been adduced suffices to show that there is this fundamental difference between them, namely, that by the slow cumulative action of the organic medicines we produce organic changes in the nutrition of the body, either in its fluids or in its solid tissues. By the functional medicines we produce no organic change whatever. By repeated dosing with them we only do over and over again what we did with the first dose. Functional medicines, therefore, never cure any disease. The most they can ever do is occasionally to break a nervous habit. Hence, as the neurotics belong to the class of functional medicines, no true nervous disease can be cured by a neurotic. All a neurotic does in any nervous disease is to relieve some symptom of that disease, leaving the disease itself the same as before. A man may have taken a thousand doses of stramonium for his asthma, but the thousandth dose can do no more than the first dose did, namely, relieve the symptom spasm, but in no way modify the disease (asthma) itself.

The only difficulty which I have experienced in demonstrating these principles has arisen from a slowness on the part of some minds to recognize what the difference between the function of an organ and the organ itself is. How an agent, for example, like veratrum viride, or like digitalis, can act on the function of the heart and not on the heart itself, is to them puzzling. But this should be no more puzzling than the common fact that a man may act on his brain for years with powerful doses of opium or of tobacco and yet not affect that organ itself enough to furnish the least clue for the most skilled microscopist to distinguish the brain of an opium or tobacco smoker from that of one who never took either of these poisons. For this difficulty the most commonly advanced hypothesis is that specific organic changes doubtless are caused in nerve tissue by these strong poisons, but that these are of such a molecular character that we have not yet attained to the requisite methods for their detection. That there must be *some* change induced is taken for granted as almost a self-evident proposition resulting from the supposed necessity that for every manifestation of nerve function there must be a corresponding physical basis in nerve matter. Moreover, this conception seems to be further supported by the undoubted fact that structural changes in any organ, including nervous organs, always manifest corresponding functional derangements, and therefore we may suppose the converse to be also true, namely, that functional derangements always have their corresponding structural changes.

But a little reflection on what function in distinction from structure really is may suffice to show that function may be either deranged or wholly arrested without structure being involved at all. For the function of an organ consists in the work that it does and in that alone. But for the working of any organ, or for that matter for the working of any mechanism, not only is structure needed, but something *plus* structure. Respiration, for example, is the function of the lungs, secretion that of a gland. Now we can either stimulate or decrease that working without affecting even molecularly the texture of the lung itself or of the gland, just as we can increase the working of a steam-engine by adding more coal, or stop it by putting the fire out, without in either case affecting the structure of the iron mechanism itself. In an oil-lamp also we may have its function of giving light much disturbed by adulteration of its oil, from diminution of its light to veritable explosion, without its own mechanism, either in its wick or in any other part of its apparatus, having anything wrong about it. It is just as true in this case that any damage to the structure of the lamp may correspondingly affect its light-giving function, but that does not prove that whenever it is disturbed in its lighting power some alteration must have happened in its structural parts.

The lamp needs for its function good structure first, but also something else. The nerve-cell likewise needs normal specially differentiated protoplasm first, but also something else, and which something else may be so deficient or deranged that the cell function will be correspondingly abnormal, no matter how normal the protoplasm itself be.

I do not see why, therefore, these illustrations do not hold good in the case of functional derangements in the *living* mechanism. We have a number of affections which in the last analysis seem to be wholly disorders of function. We say last analysis, because no methods yet discovered of investigation carry us farther than the determination of a functional derangement. Every known mode of examining structure fails of demonstrating in them the least characteristic departure from structural integrity; and yet to many minds it seems unphilosophical to rest content with the term "functional." They insist that every functional derangement must have a corresponding anatomical change to which it is due and which will account for it, and they look forward to the time when the progress of our knowledge will banish the term functional from medical terminology altogether by giving us in the case of epilepsy, hysteria, migraine and other now-named functional affections the proper anatomical designation for them. But this view arises wholly from the conception that nerve-cells work spontaneously by virtue of their organization, and therefore that when they seem to work abnormally something must have gone wrong with the arrangement of their physical molecules. It seems to be overlooked that without a constant supply of a material or materials for their working, nerve-cells must remain as inactive as a gun without its powder. If the powder be too small in quantity, or defective in making, or has been wet, all the unsatisfactory working of the gun therefore was from no fault in *it*, and why may not a nerve-cell work badly from no fault in it, but solely from deficient or poisoned function pabulum?

This question is not one of theoretical, but of practical importance. If every functional nervous disease is really due to a definite morbid change in either nerve-cell or nerve-fibre, then we must continue to search in nerve-cell or in nerve-fibre for that change and for its causation. If, however, such nervous affections are not at all to be traced to faults of structure, but rather to disordered sources of nerve energy, then we must look *elsewhere* than to the nervous system for both the causation and for the remedying of these disorders. But in examining the conditions under which manifestations of energy take place, we are met at the outset by the fact that the relations of energy to structure are in no instance yet known to science, not even in the so-called mechanical forces. Our knowledge of such relations is purely empirical. Why electricity, for example, will traverse an iron rod but not a glass rod, we neither know nor can explain. It does not seem philosophical, therefore, to expect that in the case of nerve-function we are going to discover its structural relations any easier, and certainly not in disordered function, when we have not the slightest clue to the physical basis of a normal sensation, or of a motor impulse or of a thought. The structure of no mechanism for the utilization of energy ever gives the least indication, to one who inspects it, of what the thing is which energizes it. All he can do is to note its mode of working. And this is also all that one can do in those disorders of nerve-function which we can induce artificially by administering functional medicines. What it is that hydrocyanic acid does to a group of cells in the medulla we can only tell by describing the resultant disturbances of nerve-working, and there we must stop. But equally in those functional disturbances which cause a convulsion or a neuralgia, all we can do is to observe rather than to explain. We are not even assisted by noting how much the structure is worn by its working. Liebig erroneously thought that the energy of the muscle-cell was generated by its own self-expenditure, and hence that muscular exertion might be measured by the amount of urea formed, and there are some who still speak of the nerve-cell generating its force by using itself up in the process. But we now know that we might as well explain the flight of a bullet by noting how much the gun was worn by its discharge.

Regarding our subject, therefore, from the empirical standpoint of clinical observation, which is the only practical one, the question then arises, are there any features which distinguish supposed functional nervous diseases as a class so plainly that we can conclude from these features that they are distinct in kind from organic nervous diseases? If so, what is the significance of those distinctions, and to what conclusions do they point as to the essential characters of these disorders?

There is one distinction which has always seemed to me of fundamental import, and it is this: that no structural or organic nervous disease is ever truly *intermittent*. A hemiplegic may show a greater degree of weakness one day than another, but he is always hemiplegic nevertheless. A patient with fully developed locomotor ataxia may vary considerably in his symptoms from day to day, but never is he so much better that no one would be able to detect a sign of disease in him. And so with any of the other nervous diseases characterized by structural changes in nerve-tissue. Indeed it is inconceivable how it can be otherwise. A positive loss or degeneration in nerve-cells or nerve-fibres must show as closely corresponding defects in the use of those textures as in the case of loss or degeneration in muscle or bone. But quite otherwise is it with true functional nervous diseases. The most skilled nervous specialist may be wholly unable to suspect that a man whom he meets in company will within an hour terrify the room full of people by falling in a violent epileptic fit; or that the vivacious lady near him will be prostrated the next day with a severe sick-headache. Nothing, in fact, seems more complete than the disappearance of all signs of any disease, nervous or otherwise, in many patients with pronounced and definite functional nervous affections during the intervals between their attacks. We might as well expect to detect by our means of exploration whether a given person be avaricious or generous as whether, in many typical cases of functional disorders, they are subject to convulsive or to neuralgic paroxysms, and it is probable that anatomy will never be able to tell us how these fits happen according to structural nervous changes, until it is also able to give us the structural anatomy of cupidity or of benevolence.

But as it is difficult to imagine how an organic nervous disease can be ever truly intermittent, so it follows that a truly intermittent disease cannot have an organic basis in the nervous system. This proposition is in no way invalidated by citing those cases of epilepsy which accompany an organic lesion within the cranium, such as a pachymeningitis, syphilitic or traumatic, and which in some instances have been relieved by a surgical operation. All that can be said for the causation of the epilepsy in such instances is that any abnormal or simply unusual afferent impression, whether proceeding from an intercranial or from an extracranial focus, may cause epilepsy; as, for example, a case of severe and protracted epilepsy which supervened upon a wound of a testicle and which was cured by the removal of that testicle. Every afferent impression to which the affected nerve-centres are wholly unaccustomed may be dangerous in this way, as witness the numerous published cases of fatal status epilepticus caused by injections for washing out the pleura and also after washing out the stomach. In fact organic changes within the skull, if they occasion epilepsy, do so on just the same principle that a tapeworm in the intestine may do likewise, and they do not, therefore, afford any indication that this functional disease has at any time a true specific organic basis.

If, therefore, we have any supposed functional nervous disease, whose manifestations are continuous, and not intermittent, the presumption becomes strong that it has an organic basis, even though such has not been yet demonstrated. Paralysis agitans, for example, comes within this category, and recent investigations seem to render this surmise correct. Chorea, on the other hand, will, we think, turn out to be an exception which proves the rule. The presence of a toxic element in the blood, rather than of an organic change in the nervous system, is becoming more and more probable as the commonest cause of this affection. The great frequency of carditis in choreics, as shown by Osler, even though they have never given a history of rheumatic seizures, strongly supports the view, which I have long held, that the rheumatic poison may, in early life, manifest itself in no other way than by nervous symptoms. In the case of gout, we know that its poison often ceases in the adult to develop articular symptoms and to attack nerve-centres instead. I have a patient who can date the particular day, more than ten years ago, on which that happened after a profound nervous impression, and he has been troubled ever since with the most intractable and varied functional nervous disturbances. That the nervous system of children may therefore be specially susceptible to the rheumatic poison, more so than their articular textures, has nothing inherently improbable in it, especially as with numbers of them we find the heart also more readily affected than the joints. In common with many other observers have I been repeatedly struck with the proneness of some children to develop carditis when other signs of the presence of rheumatism, including arthritis, were but little pronounced, and this fact alone takes away much of the value of some statistics which have been published of the occurrence of chorea without rheumatic antecedents. The case indeed just cited, of the transference of gout from the joints to the nervous system from nervous shock, suggests an analogy with the often alleged origin of chorea from fright.

In severe acute functional nervous diseases, the profession, following the clue afforded by hydrophobia, has been led to look elsewhere than to the nervous system for the specific cause, and in the case of tetanus has found it. But on the same principle we ought to search likewise for the cause of Landry's paralysis. Anyone under the domination of the anatomical theory, who may see a case of this formidable disease and then watch the steady but speedy ascent of the palsy until bulbar symptoms successively develop, will feel sure that a fearfully rapid disorganization of nerve-centres is progressing under his observation. But after death nothing is found in either the peripheric or in the centric divisions of the nervous system that tells any consistent story. One or two isolated observations of limited peripheric changes comprise all the trustworthy nervous pathological anatomy of acute ascending paralysis. Other examinations by most competent investigators have shown no more certain indications how death was caused than examination of the medulla shows how hydrocyanic acid kills. On the other hand, I once had a patient with that toxic paralysis which follows diphtheria, die with many of the typical symptoms of Landry's paralysis. And it is not without significance that in nearly every autopsy of this affection, enlargement of the spleen, and often of the mesenteric glands, has been found, suggestive of a poison in the blood, rather than of an organic nervous mischief as an explanation of the mortal issue.

If, therefore, such acute functional affections, severe enough to be terribly fatal, run their course without a single characteristic change in nerve tissue, we can scarcely expect this change in the chronic varieties of functional diseases which have their long intervals of complete cessation. During these intervals, the nervous system goes on with as little sign of disturbance or of interference as it does in a man who gets intoxicated with alcohol only once every few weeks or so. But while this great feature of intermittency is utterly at variance with any theory of structural alteration that can be framed, it is not incompatible with certain facts which the study of functional medicine affords. By neurotics we can artficially induce some close imitations of functional nervous diseases, and cause delirium, convulsions, comas, neuralgias, paralyses and all intermediate symptoms of the kind, and note these symptoms disappear in about the time and order that a functional nervous attack develops and declines. The feature of intermittency would then correspond to the intervals of intoxication in this respect, namely: that with analogous periodic doses of opium, for example, we would have recurrent attacks of functional derangements, giving just the same symptoms each time, with no new element developing, just as functional nervous diseases recur for years without indicating that ominous feature of progressive extension. which goes with most organic neuroses.

So far, the analogy is good enough, but it may be well urged that the toxic theory of functional neuroses can hardly hold good for those cases which are associated with a palpable organic focus of irritation, as epilepsy from malformation of the skull, or from a pachymeningitis, or in a reflex case from a renal calculus, etc. Is it to be supposed that such permanent exciting causes of the convulsions act by generating poisons? To this it may be replied that the problem of intermittent derangements with permanent exciting causes is no better explained by any other theory than that of a concurrent toxic influence, for the permanent irritant cannot of itself be enough to cause the convulsion, else the convulsion would neither intermit nor cease, but be as continuous as the irritant is. There is in every such case, the irritant and something else, and not till both act simultaneously does a convulsion occur. It is, therefore, just as easy to explain the case by saying that the permanent irritation acts by developing an idiosycransy to the operation of certain recurrent poisons in the blood which did not exist before the irritation. This is by no means a fanciful hypothesis, for the relation of the subject of idiosyncracies to neurotics can be shown to have a much closer relation to the phenomena of functional neuroses than any anatomnical facts can. Without the slighest indication to forewarn us, we may kill a patient with an insignificant dose of chloral or of antipyrine, and in a less degree we are constantly annoyed with the unexpected and undesired response of the nerve-centres of individuals to some of the most commonly prescribed drugs. This extraordinary susceptibility to certain drug poisons is almost always a limited affair, that is, limited to certain nerve-centres in that particular individual, so that one person's idiosyncrasy is against chloral but not against morphia, or vice versa. What it is that weakens the resisting power of certain centres to certain poisons only we cannot tell, but it is quite conceivable that such a weakness may be set up by a permanent sensory irritation which may cause a toxic influence to be as operative in causing a convulsion as a single indigestible article in the stomach has been known to develop the first attack of uræmic asthma.

If insight into the origin of functional nervous diseases, therefore, is not to be expected from an investigation of their structural relations, in what direction are we to look for more satisfactory indications of their true nature, and thereby of their treatment? In reply, we would begin by a single clinical illustration:

A lady consulted me for very pronounced and severe symptoms of Graves' Disease, except that she had only moderate enlargement of the thyroid and but slight exophthalmos. She had, however, an exceedingly rapid pulse, tumultuous heart action, great loss of flesh, and *persistent diarrhœa*. She did not improve under a varied medication, but at once began, literally, to get well when she was put on an exclusive diet of fermented milk. After some months, she tired of the milk and resumed ordinary diet. Her old symptoms progressively returned. She took up the milk diet again, and at once greatly improved again. She then left off the milk, and though the symptoms once more recurred with great severity, yet she could not be persuaded to resume the milk until a short time before her death, Now, it is difficult to resist the inference that both the development of Graves' disease in her case was, for a time at least, a matter of diet—but what does that fact imply?

There may be (I only say there may be) an explanation in the view that a poison was generated in her intestines during her maldigestion which acted as a vaso-motor paralyzer when absorbed into the blood. This poison may have been exceptionally active in her case either from its specific nature, or because her liver, owing to some derangement, did not destroy the absorbed poison as it should, or lastly, because her kidneys did not eliminate it as they should. Room for speculation there certainly is, but the fact still remains—diet had more control over her disease than anything else had. Here a recent observation from a series of experiments by Charrin and Roger may have some bearing.

They found that the urine of a man fed upon an exclusively milk diet lost the toxic properties of normal urine when injected into rabbits, guinea pigs, and dogs indifferently in great the proportion of one to ten. (La Semaine Médicale, 1888.)

That decompositions are constantly occuring in our digestive laboratory in the healthiest state of the body, which yet are accompanied by the formation of definite and virulent poisons, is one of the most important discoveries of modern science. As Dr. Lannder Brunton remarks,[1] "We may now indeed regard alkaloids as products of albuminous decomposition, whether their albuminous precursor be contained in the cells of plants and altered during the process of growth, or whether the albuminous substances undergo decomposition outside or inside the animal body, or by processes of digestion. Thus the poisonous alkaloid muscarine, which had only been known as obtainable from a plant, the *Agaricus muscarius*, has been discovered by Brieger to be a product of the decomposition of fish. A considerable production of alkaloids takes place in the intestines, both when the digestive processes are normal and more especially when they are disordered; at the same time, alkaloids are being formed in the muscles and possibly in other tissues. Were all the alkaloids to be retained in the body, poisoning would undoubtedly ensue, and Bouchard considers that the alkaloid formed in the intestine of a healthy man in twenty-four hours would be sufficient to kill him if they were all absorbed and excretion stopped." That these formations of alkaloidal poisons are in many instances due to the activity of specific bacteria is also demonstrated. It is thus that indol is produced out of the products of pancreatic digestion, and then sent to the kidneys to excrete as indican, as shown by Brieger. The same has demonstrated by Thudichum to be the source of the coloring principles of the urine, first formed in the intestine and then sent to the kidneys for excretion. (Lancet, Dec,, 1889.) It has even been proposed to use these facts to determine the degree in which the kidneys have been damaged in chronic Bright's disease, by noting how much less toxic Bright's disease urine is than normal urine, as an indication of the failing power of the kidneys to eliminate the poisons that come to it from the great digestive laboratory. Thus, according to Bouchard's modification of the original ratio of Feltz and Ritter, the urine of a healthy person injected into a rabbit's vein kills in the proportion of 50 grms. per kilogram of weight of the rabbit's body. But that of Bright's disease subjects is tolerated in much larger doses. Dieulafoy mentions a rabbit of 2 kilograms weight for which the toxic dose of healthy urine would be 100 grms. but which showed no discomfort until 260 grms. of the urine of a patient with Bright's disease had been injected, and even then recovered. ("Lancet," June 4, 1887.)

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[1] Pharm and Tox., p. 1co, 89.

The constant production during healthy life of these animal poisons as they can be guaged by their elimination in the urine, is shown even by their periodic variability. Thus Bouchard, ("sur la variations de la toxiüté urinaire pendant la reille et pendant la sommeil." Gaz. Hebdomadaire," April, 1886.) shows that if the day be divided into three peroids of eight hours each, the proportional quantities of poison excreted are: asleep, 3; early wakening period, 7; late waking period, 5. The urine after sleeping and waking hours also differs qualitatively as well as quantitatively. The alkaloid of the urine of sleep is *convulsive*, that of the waking urine *narcotic*. Fasting increases the toxicity of the urine. Labor and increased respiration of fresh air greatly diminishes the toxicity. We would by such facts seem to have some clue to the nocturnal character of some cases of epilepsy, also of attacks of asthma, gout, etc., during the later hours of the night. But the chief interest of these discoveries lies in the illustration which they afford of the continued liability throughout life, of the nervous system to causes of the most serious functional derangements from the uninterrupted formation in all the processes of life of active functional poisons which would operate immediately were the means provided for their elimination or destruction to become disordered.

This subject, however is so extensive that we are precluded by want of time to allude to more than a few illustrative examples. Thus one of the most suggestive formations of a poison in the body consists of the allied poisons choline, neurine and muscarine, the latter two being extremely virulent. Now choline, which has been found by Brieger to be such a common product of putrefaction, has been found by numerous investigators (Boehm, Schoeff, H. Griers, Jahns, *et al.*) very extensively in leguminous plants, as beans and lentils, in peanuts, cottonseed, hops, and therefore in beer, besides in various edible fungi. By a single substitution of a molecule of water choline is turned into neurine, a substance which has been stated by Liebrich ("Untersuch. uber Ptomaine," I., p. 32) to exist only in brain matter, but Prof. Schmidt ("Pharm. Rundschau," 1887, p. 266) has shown that when hydrochloride of choline is allowed to stay in contact with blood for some time at a temperature 30–35 C. it is converted into neurine, while Wurz ("Bielstein's Org. Chem." p. 402) has shown how choline by treatment with an acid is converted into muscarine, the alkaloid found, as stated above, by Brieger in fish. In this connection the valuable researches of Knorr ("Pharm. Zeitung," p. 366) on the molecular constitution of morphine, are interesting, as he shows the very close relationship of the latter to choline.[2]

These facts at least demonstrate that we do not have to go far to find the explanation of every symptom of functional neuroses when the system is constantly producing the agents which would inevitably occasion them all without exception, according to the varying conditions of its functional activity. Headache, muscular languor, diarrhœa, depression of the heart or palpitation, depression of the spirits, and convulsions are among the toxic symptoms, and moreover, like our familiar drug poisons, these body-generated alkaloids have their relative affinities for different nerve-functions as special and as characteristic as any of the agents of our materia medica. In fact, so close is the resemblance that they have often given rise to disputes in medico-legal cases. Thus, in the celebrated Brandes-Krebs trial, two chemists obtained from the cadaver in addition to arsenic, an alkaloid which they pronounced to be coniine, but which Otto proved only to be closely analogous to coniine and also to nicotine. Brouardel and Bautney found in the body of a woman who died from eating a stuffed goose a body which gave the odor of coniine and the same re actions of that poison with gold chloride and potassium iodide. In a criminal prosecution at Verona, Ciotta obtained from the exhumed but only slightly decomposed body, an alkaloid which he pronounced as identical with strychnine, until this identity was disproved by Selmi. So also, have morphine-like substances, others closely resembling atropine, others like digitalis, been found in similar toxical cases. ("Vaughan on Ptomaines and Leucomaines," p. 110, sg.)

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[2] For an exhaustive account of this subject consult the able and scientific paper of Prof. F. B. Power and Jacob Cambier, of the University of Wisconsin, on their "Isolation of Choline from the Bark of the Common Locust or False Acacia." Supplement "Scientific American," Mar. 15–22, 1890.

Against this auto-infection or self-poisoning we seem to be protected in great part by the liver. It is fully demonstrated now that the liver possesses a two-fold power, to prevent poisons entering by the portal vein from passing into the general circulation, for it turns back some and destroys others. Some poisons, such as curare, are sent back in large part by the bile,but with others it either decomposes them altogether or renders them in large part innoceuos,for double the quantity of strychnia, veratria or morphia is required to kill an animal if injected into the portal vein as would be sufficient if injected into the jugular vein, while no less than three times the quantity of curare is requisite (Brunton op. lit.) The remainder seems to be sent to the kidneys for elimination.

But a greater preservative still remains in the natural digestive secretions of the alimentary canal itself. In the case of the gastric juice this was shown long ago by De Haen, but the same fact holds true of the intestinal digestive juices that no better antiseptics can be found. This double function of the digestive secretions is too often overlooked, namely: that they not only digest but preserve. Any suspension or perversion of normal digestive secretion therefore, at once raises the danger of poisoning from the ready perversion of the contents of the canal to undergo fermentation when the digestive juices are deficient. Often the resulting catarrh of the intestines from the local irritation of such fermentation leads to the flux of summer diarrhœa, which to a certain extent is therefore beneficial rather than harmful. But on the other hand, this danger of auto-infection is one of the commonest attendants of fever from the rapidity with which the fever process arrests all gland secretion, including the alimentary secretions, and no one who watches the symptoms of typhoid fever can fail to note how many of them resemble those of toxic infection. As we might expect, therefore, the urine has been found in fever, especially in typhoid, (Bouchard, Lepine, Guerin, Brunton) to be much more toxic than normal urine. Mr. A. P. Luff, Lecturer on Toxicology, St. Mary's Hospital, London, ("Brit. Med. Jour.," July 27, 1889) claims to have found a distinct alkaloid in typhoid fever and another in scarlet fever.

Closely allied to the genesis of functional diseases are the problems connected with those varied morbid states of the blood to which the general term anæmia is given, and in this connection, we can only refer to the admirable lectures on the "Pathology of Pernicious Anæmia," by Dr. W. Hunter, which form the most important recent contribution to medicine by British investigators. ("Lancet," Sept. 22, 29; Oct. 6, 1888.) After demonstrating that this is a specific disease on account of its showing a characteristic structural lesion, namely: the deposit of iron in the liver cells, he says: "In pernicious anæmia the seat of disintegration is chiefly the portal circulation, more especially that portion of it contained within the spleen and liver, and the destruction is effected by the action of certain poisonous agents, probably of a cadaveric nature, absorbed from the intestinal tract." This hypothesis is rendered all the more probable by the febrile character of this affection which has always served with me to distingush this from other forms of serious anæmia with which it is often confounded. In later communications published in "The Practitioner," (see also "Lancet," Jan. 11, 1890) Dr. Hunter adduces still further confirmations of the view that pernicious anæmia is due to a hæmolytic process induced by some ferment in the gastro-intestinal tract by observations on the excretion of pathological urobilin, of blood pigment, and of urine in this disease. In a typical case which he examined, he draws attention to the exceedingly high color of the urine although the specific gravity remained low. Bile pigments were not the cause of this coloration, for spectroscopic examination showed it due to that form of pathological urobilin which MacMunn proved to be distinct from the urobilin of normal urine and to be formed by excessive elimination of bile into the intestine. Dr. Hunter then instituted an inquiry into the excretion of iron in the urine in health and in disease, and he estimates the daily health average as from 3 to 5 millegrammes. He found that the administration of iron by the mouth hardly, if at all, increased the amount of iron excreted. In one observation in health the iron excreted amounted to 5.65 mm., in one case of chlorosis to 1.71 mm., in another 1.96, and in a third 1.61, considerably lower than the average but consonant with the diminished richness of the blood in hæmoglobin characteristic of this affection. But in the case of pernicious anæmia, the daily average of iron excreted for about three weeks in the urine amounted to the great figure 32.26 millegrammes.

In the afebrile disease, chlorosis, on the other hand, many modern investigators ascribe the blood-change to absorption of poisons from retained fecal accumulations. Sir Andrew Clark is such an advocate of this theory that he proposes to term chlorosis, fecal anæmia. There are some facts, however, in the genesis of this disease which seem to me to lie back of the constipation of chlorotics, and which have an important bearing on functional nervous diseases as well. In not a few conditions we seem to have an illustration of a vicious circle of interacting causes of disorders of digestion, beginning with a reflex nervous irritation suspending or perverting the digestive secretions and also paralyzing the intestinal movements, while these effects in turn become causes of the formation and the retention of excrementitious matters, and thus of auto-infection. When I first entered on the practice of medicine I met a remarkable instance of the kind in consultation with two medical friends, who also called in the late Dr. White, of Buffalo, professor of obstetrics in the Bellevue Hospital Medical College, New York. The particulars of the case I published in the "Transactions of the New York State Medical Society," for the year 1867, p. 148. The patient, being a girl, aged seventeen, who, after a suppression of the menses, induced by a wetting in a cold shower, had first all the symptoms of intestinal obstruction with repeated fecal vomiting, but with no pain. By the administration of active purgatives some scanty movements would be obtained; but though calomel (with jalap) was freely given, yet the dejecta were uniformly so white as to resemble lime plaster. (We now know that this absence of color in the fæces denoted suppression of the pancreatic as well as of the biliary reactions.) If purgatives were not given, the constipation would continue, soon to be followed by stercoraceous vomiting. Ere long, however, a new train of symptoms set in. First, the urine was suddenly suppressed, and the death of the patient was daily anticipated; but, instead of that, a profuse salivation occurred, amounting to about three pints daily, accompanied by a copious flow of tears, not caused by any emotion whatever. In fact, the mind of the patient was remarkably clear and composed from first to last, nor did she ever present a single symptom which could be properly termed hysterical. This combined salivation continued for about three days, and then ceased, whereupon the kidneys resumed their proper action for a few days more, and then stopped again, when immediately the saliva and the tears began to flow as freely as before. This alternation between these widely separated glands finally became a regular feature of the case, the change from one to the other sometimes occurring as often as on alternate days until death took place, in a little over two months from its first occurrence. Meanwhile the stercoraceous vomiting similarly alternated with small white alvine discharges, and the stomach refused to retain anything, so that life was maintained by nutritive enemata.

Now, in this case, and in others similar to be found in medical literature, we have but an extreme illustration of the power of reflected irritation from pelvic nerves to derange both the whole series of the alimentary secretions and of the gastric intestinal movements, yet not differing except in degree from the common derangements of the early months of pregnancy. But just such influences may precede, and as I believe actually do precede, the development of the hysterical status. Why is it not a probable deduction that in the usually perverted and disordered intestinal digestion of hysterical patients we may have all the conditions needed for a veritable intoxication of the blood with functional poisons to which, rather than to an occult fault in nerve-centres, the symptoms of the disease are due? Certainly, since I have treated hysteria with that conception in mind, by repeated purgation and the administration of intestinal antiseptics, I have had, as I think, much better results than by dosing them with many of the old-fashioned antispasmodics.

The same I can say of my treatment, in the main, of migraine. The frequent sallow complexion and the high-colored urine of these patients, on the subsidence of an attack of sick-headache, not to mention the early supervention of fermentative eructations in this affection, long ago led me to look upon the majority of these cases, not as instances of "nervous storms," but of cases of imperfect digestion; and it is a question whether most of our reputed remedies for this form of headache do not act chiefly by virtue of their antiseptic properties. The fact that many of these cases present a history of marked hereditary predisposition rather favors the toxic theory, for both rheumatism and gout are equally characterized by heredity. The phenomenon of periodic explosion of the attacks, however, which this affection shows in common with some cases of epilepsy, is closely analogous with the occasional action of some functional poisons. For a long time I was inclined to be incredulous about the cumulative property of digitalis, simply because, like all incredulity, mine was based on nothing but the failure of my own experience to furnish a case, though I had prescribed digitalis largely. But one patient with phthisis, to whom I had given this drug in divided doses for about a week, banished my doubts ever after by a veritable explosion of the symptoms of that poison such as I will not soon forget. The same development is said to occur occasionally with strychnia. But the most marked illustration of this property of neurotics I had from a prescription, which I used, some ten years ago, quite extensively, in both hospital and private practice, for the reduction of temperature in phthisis, and which consisted of two drops of the tincture of aconite-root, with one drop each of the tincture of veratrum viride and of the fluid ext. gelsemin., given three times a day. It seemed to answer the indication very well during some two years' trial, but I was obliged to abandon it, owing to sudden and alarming symptoms of collapse occurring in five cases, after some two weeks' or so administration, three of them in the Charity Hospital and two in the Roosevelt Hospital. After recovery from these prostrations, however, the temperature remained down for prolonged periods in each of the patients, in no case less than two weeks and in one for three months.

I had intended to speak fully on the bearing of these considerations on the treatment of epilepsy, but time fails me now, and I will have to defer that to another opportunity. Of course, with such a great variety of afferent exciting causes to induce the attacks, one cannot claim that epilepsy can be ascribed chiefly to infection by functional poisons in more than in a certain proportion of cases. Yet that a great many epileptics cannot be relieved until this source of functional derangement is detected and remedied, I fully believe from results in treatment which in some instances have been too pronounced to admit of doubt. Among other questions, I always ask whether a bad breath is noticed, either as preceding the attacks or as occurring during them. This symptom I find to be quite common, while in other cases constipation or diarrhœa is so associated, and not infrequently such clues have proved of the greatest value in directing the treatment.

The course of medical progress has been aptly likened to a spiral ascent, opinion repeatedly coming round toward former positions, but each time above, rather than at the level of the older views. The doctrines of cellular pathology and the great increase in the knowledge of the structural changes of disease, especially in the case of the heart, lungs, and kidneys, with their consequent aids to diagnosis, have displaced for years the humoral pathology of our predecessors. These advances have caused the stomach and bowels to lose much of the importance which they held in the minds of the old physicians as the chief centres of the processes both of life and of disease. Now, however, that chemistry is asserting her claims to be heard, as well as anatomy, the set of the current is once more in the old direction. It is curious, therefore, to find this tendency re-enforced even from the side of anatomy. It sounds strangely like a distant echo of the ancient teaching, that the origin of feelings, emotions, and moral characteristics is in the bowels, to find St. Paul, with his exhortation to put on "bowels of mercies," confirmed in a way by Dr. J. Bland Sutton, who says that "he is convinced that the spinal cord and brain of vertebrata have been evolved from what was originally a section of the alimentary canal; in other words, the central nervous system is a modified piece of bowel" (!).[3] Dr. Gaskell also comes to the same conclusion by a different course of research, and states that "the tube which primarily represents the central nervous system in the vertebrate embryo must be regarded as a disused segment of the primitive alimentary canal."[4]

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[3] Brain, vol. x., p. 432.

[4] Ibid., vol. xi., p. 336.